IN THE UNITED STATES DISTRICT COURT
FOR THE SOUTHERN DISTRICT OF WEST VIRGINIA
AT CHARLESTON

IN RE: ETHICON, INC., PELVIC REPAIR SYSTEM PRODUCTS LIABILITY LITIGATION THIS DOCUMENT RELATES TO:	**Master File No. 2:12-MD-02327** **MDL 2327** **JOSEPH R. GOODWIN** **U.S. DISTRICT JUDGE**
ETHICON WAVE 1 CASES LISTED IN PLAINTIFFS' EXHIBIT A (DOC. 2081-1)	

MEMORANDUM IN SUPPORT OF DEFENDANTS' OPPOSITION TO PLAINTIFFS' MOTION TO LIMIT OR EXCLUDE CERTAIN OPINIONS OF ETHICON, INC.'S EXPERT DEBRA FROMER, M.D.

Defendants Ethicon, Inc. and Johnson & Johnson (collectively, "Ethicon") respectfully submit this Memorandum in Opposition to Plaintiffs' Motion to Limit or Exclude Certain Opinions of Debra Fromer, M.D. ("Dr. Fromer").

INTRODUCTION

In seeking to bar certain of Dr. Fromer's opinions, Plaintiffs mischaracterize the scope of her opinions as well as the evidence on which they are based. When Dr. Fromer's opinions are considered within their proper scope, and in light of the broad sources of evidence that inform Dr. Fromer's opinions — most notably Level 1 peer reviewed medical literature — her opinions should survive Plaintiffs' challenge. Indeed, as an experienced pelvic surgeon who has performed a comprehensive analysis of twenty years of medical literature, her opinions would be very instructive to the jury and should be admitted at trial.

DR. FROMER'S PROFESSIONAL BACKGROUND

Dr. Fromer is board certified in Urology and Female Pelvic Medicine and Reconstructive Surgery.[1] Dr. Fromer attended Tufts University School of Medicine and graduated with honors in 1998. [TVT-O General Expert Report of Dr. Fromer ("Fromer TVT-O Report"), Doc. 2081-2, pg. 1]; (Ex. A, Prolift General Expert Report of Dr. Fromer ("Fromer Prolift Report"), pg. 1). Dr. Fromer completed her general surgical training in 1999 at Columbia Presbyterian Medical Center, where she stayed to complete her training in Urology in 2003. [Fromer TVT-O Report, Doc. 2081-2. pg. 1]; (Ex. A, Fromer Prolift Report, pg. 1). Dr. Fromer subsequently joined the faculty practice at Hackensack University Medical Center where she has been practicing for the last 11 years. [Fromer TVT-O Report, Doc. 2081-2. pg. 1]; (Ex. A, Fromer Prolift Report, pg. 2). She is currently the Chief of Female Pelvic Medicine and Reconstructive Surgery at Hackensack University Medical Center, the Program Director for the Fellowship in Female Pelvic Medicine and Reconstructive Surgery at Hackensack University Medical Center, and Assistant Professor in Urology at Rutgers, the State University of New Jersey. [Fromer TVT-O Report, Doc. 2081-2, pg. 1]; (Ex. A, Fromer Prolift Report, pg. 1). Female patients make up 90% of her practice, which is largely dedicated to treating women for pelvic health conditions such as incontinence, prolapse, urinary tract infections, sexual dysfunction and pelvic pain. [Fromer TVT-O Report, Doc. 2081-2, pg. 2].

She has performed over 1,000 anti-incontinence procedures, the vast majority of which involved polypropylene mesh slings, including hundreds using Ethicon's TVT-O device. [3/29/2016 Deposition of Debra L. Fromer ("Fromer Dep."), Doc. 2081-3, at 55:25-56:1; Fromer TVT-O Report, Doc. 2081-2, pg. 1]. She has also performed over 500 surgical procedures to

[1] Plaintiffs inaccurately state that Dr. Fromer was trained in obstetrics/gynecology. [Pls. Mov. Br., Doc. 2084, pg. 2]

treat pelvic organ prolapse, the majority of which include some form of polypropylene graft, including hundreds of Prolifts. (Ex. A, Fromer Prolift Report, pg. 2); [Fromer Dep., Doc. 2081-3, at 67:7-10].

BASES OF DR. FROMER'S OPINIONS

The first paragraph of Dr. Fromer's general reports on Prolift and TVT-O sets forth the sources of information and evidence that form the bases for her opinions: information and knowledge acquired from (1) education, (2) training, (3) personal experience in private practice, (4) teaching, (5) discussion and interaction with other pelvic surgeons in professional activities and conferences, (6) research, and (7) review of medical literature. [Fromer TVT-O Report, Doc. 2081-2. pg. 1]; (Ex. A, Fromer Prolift Report, pg. 1).

Despite her extensive surgical experience implanting Prolift and TVT-O, even a cursory review of her general expert reports reveals that her opinions in this litigation are based largely on her extensive review of medical literature, including Level 1 evidence such as Cochrane Review meta-analyses assessing thousands of patients, and numerous randomized controlled trials, not to mention public statements by the FDA and medical societies in the fields of urology. Two-thirds of Dr. Fromer's TVT-O general report (pgs. 9-28) are dedicated to a detailed analysis of the extensive clinical literature that has evolved over twenty years on midurethral slings and TVT/TVT-O in particular, with specific focus on potential complications. Similarly, two-thirds of her Prolift general report (pgs. 10-35) are dedicated to a detailed review of the peer reviewed medical literature (including meta-analyses and randomized controlled trials) assessing Prolift, other surgical treatment options for prolapse and potential complications. By contrast, a much smaller portion of her reports is dedicated to her personal surgical experience or to the complication rates she has observed solely in her patients.

LEGAL STANDARD

Ethicon incorporates by reference the standard of review for *Daubert* motions as articulated by the Court in *Edwards v. Ethicon, Inc.*, 2014 WL 3361923, at *1-3, 2014 U.S. Dist. LEXIS 92316, at *3-8 (S.D. W. Va. July 8, 2014).

ARGUMENT

I. DR. FROMER'S OPINIONS DO NOT EXCEED HER QUALIFICATIONS.

A. Dr. Fromer should be permitted to opine on the clinical impact of the TVT-O and Prolift meshes *in vivo*.

Plaintiffs first seek to bar Dr. Fromer categorically from providing any opinion related to biomaterials or pathology on the grounds that she is not specifically trained in these fields. To be clear: Dr. Fromer does not seek to opine regarding any process that occurs on a microscopic level *in vivo*. Rather, Dr. Fromer's opinions on materials and pathology issues are limited to the *clinical impact* of those alleged microscopic processes based on the detailed review of medical literature that she has conducted, as well as her surgical experience with well over a thousand patients. [3/29/2016 Fromer Dep., Doc. 2081-3, at 55:25-56:1, 67:7-10]. Such opinions are entirely appropriate.

For example, Dr. Fromer's opinions are that a chronic foreign body reaction is expected to occur on a pathologic level, but that, "[i]n clinical use, this inflammatory process has little to no clinical relevance. As a surgeon who has seen this tissue reaction in weeks to months to years after placement for a variety of reasons, not necessarily pathologic, I can attest to the fact that this reactive tissue response is predictable and consistent from patient to patient." [Fromer TVT-O Report, Doc. 2081-2, at pgs. 18-19]; (Ex. B, Maher et al (2016) Summary Cochrane Review: Transvaginal mesh or grafts compared with native tissue repair for vaginal prolapse; Ex. C, Ford

et al (2015) Full Cochrane Review: Mid-uretheral sling operations for stress urinary incontinence in women).

Beyond her personal surgical experience, in arriving at her opinions, Dr. Fromer has reviewed hundreds of published studies, in part to find substantiation in the clinical literature for Plaintiffs' claims regarding cytotoxicity, degradation and chronic inflammation. (Ex. D, Reliance list to Dr. Fromer's General Reports). With respect to these issues, her opinions derive from what she has concluded is an absence of evidence in the medical literature to support Plaintiffs' theories. While this Court has observed that "[a]bsence of evidence is not evidence of absence," *Tyree v. Boston Scientific Corp.*, the observation only holds true where a cursory inquiry of the evidence has been made. 54 F. Supp.3d 501, 583 (S.D. W. Va. 2014). For instance, if a physician is relying merely on her own experience to opine that a particular risk does not exist, the methodology may be flawed. However, where a physician examines the evidence outside of her own experience, analyzing studies and literature and Level 1 evidence, the stronger the conclusion becomes that there is no risk. Thus, while absence of evidence in a limited sampling pool of a single physician's experience may not be proof of absence, absence of evidence in a large pool of scientific literature and studies, combined with the clinical experience and evaluation of many physicians and medical organizations, is sound evidence of absence.

Her opinion on cytotoxicity is one example of an opinion rooted in her review of medical literature:

> If the PROLENE mesh used in TVT and TVT-O had the dangerous properties postulated by its adversaries, it would likely cause many more negative clinical consequences than what has been described in the medical literature over the last 20 years of use. To the contrary, in clinical use, the mesh used in these slings is effective with extremely low complication rates and minimal morbidity, as is evidenced by the large body of literature supporting this. Therefore, despite reports of in vitro

> "cytotoxicity," there is no such evidence of clinical, in vivo "cytotoxicity" in the medical literature.

[Fromer TVT-O General Report, Doc. 2081-2, pg. 18].

Dr. Fromer's opinion regarding alleged degradation is similarly based on an absence of proof in the medical literature of any clinical impact upon patients:

> There is no medical literature supporting the notion that polypropylene mesh "degrades" in any clinically significant way. . . . Given the large body of literature on the long-term efficacy of polypropylene slings with over 17 years of follow up, it stands to reason that the polypropylene in slings, and in Prolift, does not degrade in any substantial or clinically significant way.

(Ex. A, Fromer Prolift Report at pgs. 41-42). Dr. Fromer's report then proceeds to consider and deconstruct the Clave 2010 study, which is the primary study that Plaintiffs cite in support of their degradation theory. (*Id.*).

This Court has already found that the same methodology employed by Dr. Fromer survives *Daubert* scrutiny. In *Watkins v. Cook, Inc.*, 2015 WL 1395773, at *13 (S.D. W. Va. March 25, 2015), this Court found that a practicing urologist's "comparison of his experience to a reliable and relevant peer-reviewed study . . . is enough to open *Daubert's* gates." Also in *Tyree v. Boston Scientific Corp.*, this Court concluded that a urologist's clinical experience and review of the scientific literature, which he explained and cited throughout his expert report, "are sufficiently reliable bases" to opine that he has not seen "evidence of polypropylene degradation, systemic infection, or other unexpected reactions." 54 F. Supp.3d at 585. Thus, Dr. Fromer should not be barred from testifying regarding the lack of evidence of any clinical impact of materials issues such as cytotoxicity, degradation or chronic inflammation. Her thorough review of the medical literature on these issues combined with her qualifications render these opinions more than sufficiently reliable to be admissible at trial.

B. Dr. Fromer is qualified to testify about the sufficiency of the TVT-O and Prolift product warnings based on her extensive review of the medical literature, her substantial experience using medical devices, and her training.

Plaintiffs also seek to preclude Dr. Fromer from offering opinions on the adequacy of Ethicon's product warnings because she has not drafted any IFUs, could not recall specific details about prior consulting work, and does not believe that IFUs are the most important source of risk information that a pelvic surgeon utilizes. These are not appropriate bases to exclude her testimony.

Throughout this litigation, this Court has permitted clinicians to opine on the adequacy of Ethicon's IFUs. These clinicians have been deemed qualified based on their surgical experience, not prior experience in formulating IFUs. For instance, in *Huskey v. Ethicon, Inc.*, this Court held that plaintiffs' expert urologist Dr. Jerry Blaivas could testify about the sufficiency of Ethicon's warnings despite his lack of familiarity with the relevant FDA regulations. The Court determined that "Dr. Blaivas need not be an expert on product warnings per se," because he "is qualified to testify about the risks of implanting a TVT-O and whether those risks were adequately expressed on the TVT-O's IFU." *Huskey v. Ethicon, Inc.*, 29 F. Supp.3d 691, 718, (S.D. W. Va. 2014).

Dr. Fromer's qualifications to opine on warnings adequacy are not based only on her surgical experience, which is detailed above, but also on her extensive review of the medical literature, which has documented the risks and benefits of pelvic mesh implants. (Ex. D, Reliance list to Dr. Fromer's General Reports.) The hundreds of published studies she has reviewed include sources at the highest levels of scientific evidence, including Cochrane Review meta-analyses assessing 37 RCTs and 4,023 patients for pelvic floor repair and 81 trials and 12,113 women who had undergone midurethral slings. (Ex. B, Maher et al (2016) Summary

Cochrane Review: Transvaginal mesh or grafts compared with native tissue repair for vaginal prolapse; Ex. C, Ford et al (2015) Full Cochrane Review: Mid-uretheral sling operations for stress urinary incontinence in women); [Fromer TVT-O General Report, Doc. 2081-2, pg. 13]; (Ex. A, Fromer Prolift General Report, pgs. 19-20). They also include numerous randomized controlled trials assessing TVT-O with up to five years of follow-up, including the TOMUS trial, Laurikainen and Tommaselli randomized controlled trials. [Fromer TVT-O Report, Doc. 2081-2, pgs. 13-15]. They also included several randomized controlled trials assessing Prolift, including Altman 2011, de Silveira 2014, and Svabik 2014. (Ex. A, Fromer Prolift Report pgs. 30-31). This does not even include the hundreds of peer-reviewed published prospective and retrospective studies that Dr. Fromer has reviewed and considered. This literature review, combined with her surgical experience, renders Dr. Fromer eminently qualified to opine regarding adequacy of Ethicon's product warnings for Prolift and TVT-O.

Nor do the bases for Dr. Fromer's warnings opinions end there. As set forth in her report and list of reviewed materials, she has also reviewed and considered the FDA's Device Labeling Guidance ("Bluebook Memo"), various FDA statements regarding surgical mesh, and statements issued by numerous medical societies regarding the safety of pelvic mesh products. (Ex. D, Reliance list to Dr. Fromer's General Reports). Additionally, through her interactions with other physicians, Dr. Fromer has learned what other clinicians know, expect and experience regarding Ethicon's products. In addition to training residents and fellows as an Associate Professor and Fellowship Director on a regular basis, Dr. Fromer also served as a preceptor for TVT, TVT-O and Prolift, where she trained attending physicians in one to two hours of didactic training and two to four hours of hands-on cadaver training. [Fromer TVT-O Report, Doc. 2081-2, pg. 2]; (Ex. A, Fromer Prolift Report, pgs. 3-4).

Dr. Fromer also assisted in the drafting of warnings for a drug that was in development around eight to ten years ago called Tovias, which treated overactive bladder. [3/29/16 Fromer Dep., Doc. 2081-3, at 22:6-19, 23:3-24:20]. As a member of the consultation group formed for developing Tovias, Dr. Fromer was involved with the discussion and development of the labeling, including warnings and side effects. [*Id.* at 23:3-23]. While she cannot closely recall the details of that consultation, Dr. Fromer's experience with Tovias has contributed to her knowledge base on product warnings and further reinforces her qualification to opine on the warnings' adequacy.

Plaintiffs also argue that Dr. Fromer should be barred from testifying about warnings adequacy because she does not consider the IFU to be the central vehicle by which doctors get trained in how to perform surgery. [Pls. Mov. Br., Doc. 2084, pg. 5]. This, however, is not a legitimate basis for exclusion. In her deposition, Dr. Fromer recognized the role of IFUs and that she reviews them, but also noted that the IFU is but one means by which surgeons become informed: "surgeons should not be relying on an IFU to know what the risks, benefits, and how to use the products are [*sic*]. I believe that they should have hands-on training and not learn from a piece of paper how to do a surgery and what the complications and risks are." [3/29/16 Fromer Dep., Doc. 2081-3, at 25:13-18]. Her opinion on this point can be addressed on cross-examination at trial, but provides no legitimate basis to limit her opinions on warnings adequacy — particularly when weighed against her review of peer-reviewed medical literature, surgical experience, and the training she has received and provided on the use of the products at issue.

II. DR. FROMER'S CLINICAL OBSERVATIONS OF HER OWN PATIENT POPULATION IS BUT ONE BASIS — AND NOT THE PRIMARY BASIS — FOR HER OPINIONS REGARDING THE SAFETY OF PROLIFT AND TVT-O.

Plaintiffs seek to bar Dr. Fromer from offering opinions about the safety of Prolift and TVT-O based on her experiences with her own patient population.

Plaintiffs' argument relies in large part on deposition testimony Dr. Fromer provided in response to questioning by Plaintiffs' counsel regarding a published study she co-authored on a segment of her patient population. [Pls. Mov. Br., Doc. 2084, pg. 6]. Plaintiffs suggest that because Dr. Fromer has tracked her studied patients differently in the co-authored study from her larger body of patients, she should not be able to draw upon her knowledge from 11 years practice and over 1000 implant surgeries to inform her opinions. In support of this argument, Plaintiffs cite no decision of this or any other court. To the contrary, the law provides that Dr. Fromer's surgical experience with her patients is relevant and may be a source for her opinions. *Huskey v. Ethicon, Inc.*, 29 F. Supp.3d 691, 726 (S.D. W. Va. 2014) (finding Dr. Pramudji was qualified by her medical experience to testify whether she has observed mesh degradation in her clinical practice). More importantly, this Court has recently held in *Trevino v. Boston Scientific Corp.*, that Dr. Culligan, a defense expert urogynecologist, could testify regarding the safety and efficacy of the Uphold device despite the *Trevino* plaintiffs' argument that he could not testify "as to exact statistics about his patients," by explaining that "such detail is not required under *Daubert* to opine as to the '*large-scale* safety and efficacy of the Uphold device . . .'" 2016 WL 1718836 at *33 (S.D. W. Va. April 28, 2016). Here, because Dr. Fromer only seeks to opine on the large-scale safety and efficacy of the devices at issue, her opinions should not be excluded.

Notwithstanding, Dr. Fromer's observations of her own patient population are not the sole, or even the primary, basis for her opinions on the safety of Prolift or TVT-O. As discussed in detail in this brief and evident throughout her Expert Reports, Dr. Fromer's opinions are primarily based on her review of the highest level of peer-reviewed medical literature, including meta-analyses and RCTs, as well as her training. (Ex. D, Reliance list to Dr. Fromer's General Reports). The complication rates that Dr. Fromer cites in her reports derive from published

medical literature and not her "personal complication rate." For example, at her deposition, Dr. Fromer referred to medical studies she relied upon when asked about rates of complications:

> Question: Is it consistent with your understanding that there's a higher rate of vascular injury and bleeding associated with the retropubic device than the obturator device?
>
> Dr. Fromer: Well, why don't we just look at one of the articles quickly that I've relied upon. I'm pulling out the Schimpf study.
>
> …
>
> Question: They report out 6.0 to 39.1 percent rate of nerve injury and pain associated with transvaginal repair. Is that consistent with your understanding?
>
> Dr. Fromer: Again, it's a very wild range that's listed here. And I'm sure if you look at certain studies, you can see higher rates than lower rates. But if you're looking at the global picture, the number is probably closer to the 6 and possibly lower than the 39.
>
> Question: Okay. And that's based on the literature that you have cited here, correct? That's the basis for your opinion on that?
>
> Dr. Fromer: Yes.

[3/29/16 Fromer Dep., Doc. 2081-3, at 113:25-114:6, 119:3-15].

Ultimately, under a *Daubert* analysis, the fact that Dr. Fromer has not tracked the progress of every single patient she has treated does not bar her from drawing upon on her surgical experience as a component of her expert opinions.

III. PLAINTIFFS MISCHARACTERIZE DR. FROMER'S OPINIONS REGARDING MECHANICAL CUT MESH VS. LASER CUT MESH.

Plaintiffs wrongly suggest that Dr. Fromer has affirmatively opined that "mechanically-cut mesh performs the same clinically as laser-cut mesh," and then criticize her for having no basis in literature for this conclusion. To the contrary, Dr. Fromer's opinion is that there is no basis in the literature *to support the claims of Plaintiffs' experts* that laser cut mesh is safer than

mechanical cut mesh (or vice versa). Specifically, Dr. Fromer opined in her TVT-O general report:

> TVT has been offered in mechanically cut mesh since its inception and in laser cut mesh since 2006, enabling surgeons a choice in this property of the mesh. Though some surgeons prefer mechanically cut mesh and some prefer laser cut mesh, there is no data in the medical literature to support one type of cut over the other. Similarly, though some surgeons may feel that the mechanically cut mesh results in mesh fraying and loose particles, in my experience this fraying is clinically inconsequential and not responsible for any untoward outcome of surgery. Similarly, there is no data in the medical literature to support this claim.

[Fromer TVT-O General Report, Doc. 2081-2, pg. 18].

Therefore, it is in the context of refuting Plaintiffs' experts that Dr. Fromer testified "there is no data to support one is better than the other." [Pls. Mov. Br., Doc. 2084, pg. 8]. Plaintiffs apparently seek to exclude Dr. Fromer's testimony on this point in an attempt to divert attention from the unsupported opinions of their own experts regarding the differences between laser cut mesh and mechanical cut mesh. (Ex. E, TVT-O General Expert Report of Jerry G. Blaivas, pgs. 12-14).

Ultimately, there is no basis to preclude Dr. Fromer from challenging Plaintiffs' experts by pointing out the lack of clinical evidence supporting their assertions that the manner in which mesh is cut bears on the safety of the device.

CONCLUSION

For these reasons, Plaintiffs' Motion to Limit or Exclude Certain Opinions of Ethicon's Expert Dr. Fromer should be DENIED.

Respectfully submitted,

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CERTIFICATE OF SERVICE

I certify that on May 9, 2016, I electronically filed this document with the clerk of the court using the CM/ECF system, which will send notification of this filing to CM/ECF participants registered to receive service in this MDL.

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